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Date: December 14, 2001

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Comments: **U.S. Application No.: 08/954,771**  
**Filing Date: June 5, 1995**  
**Group Art Unit: 1646**  
**Examiner: M. Brannock**  
**Title: Vertebrate Tissue Pattern Inducing Proteins and Uses Related Thereto**

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:  
Ingham et al.

Serial No: 08/954,771

Filed: June 5, 1995

For: Vertebrate Tissue Pattern Inducing  
Proteins and Uses Related Thereto

Attorney Docket No. HMSU-P04-006

Art Unit: 1646

Examiner: M. Brannock

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12/17/01

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and of Mail Deposit

  
Karen DiRocco

Assistant Commissioner of Patents  
Washington, D.C. 20231

**REPLY UNDER 37 CFR 1.111**

Sir:

This amendment is being filed in reply to the outstanding Office Action, mailed September 24, 2001, in connection with the above application. Please enter the following amendments:

**In the specification:**

On page 142, please replace the last paragraph with:

I  
Various fragments of the mouse *Shh* gene were cloned into the pET11D vector as fusion proteins with a poly(His) leader sequence to facilitate purification. Briefly, fusion genes encoding the mature M-*Shh* protein (corresponding to Cys-25 through Ser-437 of SEQ ID No. 11) or N-terminal containing fragments, and an N-terminal exogenous leader having the sequence M-G-S-S-H-I-I-H-H-H-L-V-P-R-G-S-H-M (SEQ ID No. 47) were cloned in pET11D and introduced into *E. coli*. The poly(His)-*Shh* fusion proteins were purified using nickel chelate chromatography according to the vendor's instructions (Qiagen catalog 30210), and the poly(His) leader cleaved from the purified proteins by treatment with thrombin.

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